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ON October 18, 2001

Charles H. Lewis
AGENT/ATTORNEY FOR APPLICANTS

October 18, 2001
DATE

P50464-1X1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Re: Jackson et al. 18 October 2001
Serial No.: 09/142,983 Group Art Unit No. 1617
Filing Date: 17 September 1998 Examiner: T. Criares
For: PLA₂ Inhibitors for Angiogenesis

Assistant Commissioner of Patents
Washington, D.C. 20231

APPELLANTS' BRIEF UNDER 37 C.F.R. § 1.192

Sir:

Pursuant to the provisions of 37 C.F.R. § 1.192, Appellants submit herewith their Brief on Appeal of the decision of the Examiner, dated January 29, 2001, finally rejecting Claims 1 to 4, 7 to 9 and 13 to 17. A Notice of Appeal was filed on April 18, 2001. Appellants file herewith a Petition for a four-month Extension of Time, which extends the time for Appellants to file their Appeal Brief until October 18, 2001.

Three (3) copies of this Brief are being filed herewith.

Please charge the fee set forth in 37 C.F.R. § 1.17(f) for the filing of this Brief to Deposit Account No. 19-2570.



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I. Real Party in Interest

The real party in interest in this appeal is SmithKline Beecham Corporation, having an address of One Franklin Plaza, Philadelphia, Pennsylvania 19103, by virtue of assignment, duly recorded in United States Patent Application Serial No. 08/468,902 recorded on November 1, 1999, at Reel 010345 and Frame 0668 by the United States Patent and Trademark Office. This application is a CPA application filed November 1, 2000 which is the §371 national stage entry of PCT application PCT/US97/04876, filed March 26, 1997, which claims the benefit of priority from USSN 60/014,244, filed March 26, 1996.

II. Related Appeals and Interferences

The central issue in this appeal is substantially similar to that in the appeal of commonly assigned U.S.S.N. 09/143,572, filed on August 28, 1998, such that for reasons of efficiency, Appellants request that these appeals be considered by the Board together. There are no other related appeals and interferences known to Appellants, Appellants' legal representatives, or the assignee which will directly affect or be directly affected by or have any bearing on the Board's decision in this Appeal.

III. Status of Claims

The instant application originally contained Claims 1 to 6. Claims 1 to 6 were found to possess novelty, industrial applicability and inventive step in the PCT application. Claims 1 and 5 were amended in the Response filed on February 11,

2000, and claims 7 to 13 were added. In the Response filed November 1, 2000, Claims 14 to 17 were added. Claims 5, 6, and 10 to 12 have been allowed. Claims 1 to 4, 7 to 9, and 13 to 17 have been finally rejected and are on appeal. The claims on appeal are set forth in the attached Appendix.

IV. Status of Amendments

The Final Office Action mailed on January 18, 2001 page 1, indicated that the Appellants' amendments adding Claims 14 to 17 were entered and that these claims, Claims 14 to 17 had been included within final rejection under 35 USC §112, first paragraph. It should be noted that the first Office Action, Paper No. 6 [January 18, 2001] in the CPA application was made final. The cover sheet, PTOL 326 form however, did not indicate that claims 14 to 17 were in the application, nor were they listed among those pending or rejected. Appellants inadvertently copied the information for their Notice of Appeal, appealing Claims 1 to 4, 7 to 9 and 13 wherein the Notice should have included rejected Claims 14 to 17. Appellants respectfully request that the Notice of Appeal and this Appeal Brief be entered with respect to all the finally rejected claims in the application, Claims 1 to 4, 7 to 9 and 13 to 17,

V. Summary of the Invention

The instant invention relates to methods of treating a chronic disease characterized by excessive, undesired, or inappropriate angiogenesis by administering

to a mammal in need thereof an effective amount of a compound which inhibits the production, transcription, or activity of the 14 kDa PLA₂ enzyme.

Claim 1 is directed to such a method, wherein the compounds were invented after March 26, 1996, the filing date of the provisional application. [Specification at pages 1, and 17.]

Claims 2, 3, and 4 are specific diseases associated with excessive, undesired, or inappropriate angiogenesis in the body of the mammal.

Claims 7, 8 and 9 are independent claims of the specific diseases of Claims 2, 3, and 4, inter alia *"A method of treating a chronic disease of diabetic retinopathy or ocular neovascularization in a mammal with an effective amount of a compound which inhibits the production, transcription, or activity of the 14 kDa PLA₂ enzyme, and wherein the compounds were invented after March 26, 1996"*.

Claim 13 is similar to Claim 1 but instead provides for alternative proviso language of "other than those compounds disclosed before March 26, 1996" instead of "invented after".

Claim 14 is similar to Claim 1 but instead provides for alternative proviso language of "wherein the compound was used before or invented after the priority date of March 26, 1996" instead of the "invented after" or "disclosed before" language of Claims 1 and 13.

Claims 15 to 17 are similar to Claims 2, 3, and 4 but depend upon Claim 14 with respect to specific diseases.

VI. Issues

The issue on appeal is:

(1) whether the Examiner erred in rejecting Claims 1 to 4, 7 to 9, and 13 to 17 under 35 U.S.C. § 112, first paragraph, for lack of antecedent basis in the specification.

VII. Grouping of the Claims

Claims 1 to 4, 7 to 9, and 13 to 17 are believed to stand or fall together.

VIII. Argument

A. New Matter Rejection

Claims 1 to 4, 7 to 9, and 13 to 17 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

Specifically, the Examiner argues that there is a lack of antecedent basis for the phrase

"and wherein the compounds were invented after the priority date of March 26, 1996 relating to future unknown compounds. There is no basis for such terminology in the specification and would not reasonable convey to one skilled in the relevant art that the inventor had possession of the claimed invention".

While not stated as such this is basically believed to be a rejection under "new matter".

Appellants respectfully submit that the Examiner has not made a *prima facie* new matter rejection. As MPEP § 2163.06 provides, a new matter rejection pertains only to an amendment of the disclosure, and not to an amendment of the claims. Because Appellants have not amended the specification to add the date restriction, such a rejection is inappropriate.

Even assuming, *arguendo*, that the Examiner has made a *prima facie* new matter rejection, Appellants assert that the date restriction recited in the pending claim is supported by the as-filed specification in the section under the title for Related Information in their claim to priority [see page 1 of the specification]. Furthermore, this priority date is supported by the application because the priority date is what the Examiner uses to determine which references constitute prior art with respect to the instant application. Accordingly, Appellants assert that the choice of the date of March 26, 1999 in the provisos of the pending claims is both logical and expressly supported by the instant specification.

Moreover, Appellants are permitted to narrow their claim scope by inserting these date restrictions, such that the claims cover a sub-set of what was disclosed in the as-filed application. As the C.C.P.A. held in *In re Johnson*, 191 U.S.P.Q. 187, 195-96 (1977), it is perfectly legitimate for an applicant to claim less than his full scope of disclosure, since it is for an inventor to decide what bounds of protection he will seek. Likewise, the C.C.P.A. indicated, in *In re Wertheim*, 191 U.S.P.Q. 90, 97

(1976): "That what applicants claim as patentable to them is *less* than what they describe as their invention is not conclusive if their specification also reasonably describes that which they do claim." Because the instant specification describes what an inhibitor of the PLA₂ enzyme is, how to characterize the PLA₂ enzyme (as well as its being well known in the art), how to screen for them [page 14, line 36, and page 15 of the specification], and how they can be used as therapeutics [pages 1 to 4, and 12 to 15 of the specification], Appellants contend that the specification does provide an adequate written description of what they are now claiming. Therefore, under the holdings of both *In re Johnson* and *In re Wertheim*, Appellants submit that the recitation of the date restriction in the pending claims is a permissible way for them to limit the pending claims.

Appellants also assert that a proviso, such as the date restrictions recited in these claims, are of a type of negative claim limitation which is permissible. It is well settled that the inclusion of a negative limitation in a claim does not render the claim *per se* indefinite, as long the claim scope is not unduly broad or uncertain. *See* MPEP § 706.03(d).

That being said, Appellants submit that one of skill in the art would readily understand what is meant by the date restriction in the pending claims. Whether the inventor or the public can define and list the entire set of compounds that are covered by the instant claims is not dispositive of whether the inventor had possession of the claimed invention at the time of filing. This specification clearly provides to the skilled artisan a listing of compounds which have been found to be suitable inhibitors of the

PLA₂ enzyme. These compounds come from many structurally diverse, and different pharmacophores or classes of compounds. Appellants invention is not the discovery of a new class of inhibitors of the 14 kDa PLA₂ enzyme, but instead the discovery that inhibition of the 14 kDa PLA₂ enzyme can be used to treat a chronic disease which disease is characterized by an excessive, or an undesired or an inappropriate angiogenic component [page 11, line 27 to 36, and page 12, lines 1 to 4] regardless of the class of compound used. A model of inflammatory angiogenesis is shown in page 12, lines 5 to 33, page 13 and page 14, lines 1 to 34 of the specification].

When a scientist is conducting research in a particular therapeutic area, such as inhibitors of the 14 kDa PLA₂ enzyme, it is a common practice for that scientist to continually conduct art-based searches to determine whether a discovered compound is novel. Such searches are very simple to carry out, and they can be based on a chemical structure, a compound name, functional terminology, *etc.* Therefore, if a scientist or other member of the public wants to determine whether such a compound falls within the scope of the instant claims, he or she would merely need to conduct an art search on the compound or a small number of compounds in question, and not the entire scope of possible compounds encompassed by the claims.

Nonetheless, issued claims in the chemical field routinely place some level of burden on the public to determine whether a given compound or other invention reads on a claim of a given patent. For instance, in the chemical arts, dependent claims that define possibilities for multiple substituent groups are common, *i.e.*, “wherein R₁ can

be a, b, c, . . . ; R₂ can be m, n, p” Such claims can encompass a colossal number of compounds, possibly numbering in the billions or trillions.

Moreover, claims in other technical fields similarly place some burden on the public to determine claim scope. One example of such a claim in the biological arts is a claim that recites a polynucleotide in terms of what sequences it will hybridize with under stringent conditions. Also, in the biotechnology area, claims to a polynucleotide having 95% identity to the polynucleotide of a reference sequence disclosed in the application are routinely issued. In order to have such “% identity” claims allowed, the definiteness requirement does not obligate the inventor to exhaustively write out every possible nucleotide sequence that would be encompassed by such a claim. Also, in the mechanical arts, means-plus-function claims place some burden on the public to determine which structures, materials, or acts constitute equivalents to those defined in terms of their function in the claims.

Appellants assert that the language used in their date provisos largely mirrors the language of 35 U.S.C. § 102 (a). Specifically, the phrases “known before” and “used before” have a statutory basis, and the USPTO Examiners have become accustomed to searching for art that meets these criteria. Therefore, Appellants submit that these phrases sufficiently convey the necessary information to the public, and define the scope of the instantly claimed methods of treatment.

Furthermore, as a matter of public policy, the U.S. Patent & Trademark Office has been issuing claims such as those pending in the instant application. These claims, commonly referred to as “mechanism of action claims” have issued in a

number of patents. For example, the Appellants include copies of the following U.S. Patents, all of which contain mechanism of action claims: US 5,403,847 (attached as Exhibit 1); US 5,677,312 (attached as Exhibit 2); US 6,048,850 (attached as Exhibit 3); US 5,830,850 (attached as Exhibit 4); US 5,587,384 (attached as Exhibit 5); and US 5,648,373 (attached as Exhibit 6).

Exhibit 6 is believed to be directly relevant to the types of claims at hand as the claims of US Patent No. 5,648,373 relate to methods of treatment in a related area, inflammation, and have a broad based functional mechanism of action means:

"A method for treating an inflammatory component of a disease or disorder mediated by the lipid inflammatory mediators, arachidonic acid, its metabolites, and/or platelet activating factor (PAF), which method comprises administering to a mammal in need thereof *an effective amount of a compound which inhibits lipid mediator production by blocking the production, activation or action of Coenzyme A-independent transacylase (CoA-IT)*".

It should also be noted that both US Patent No. 5,648,373 and the instant invention share a common inventor and a common assignee, SmithKline Beecham Corporation.

Therefore, the Appellants submit that they are merely adding a date limitation to a type of claim which the U.S. Patent and Trademark Office has allowed and been allowing on a regular basis.

Appellants have filed a number of compound and method of use applications in the field of PLA₂ inhibition, such as US 5,545,669 [WO 95/33461], WO 95/33462, WO 95/33460, WO 95/33458, WO 95/33715, WO 95/33713 and WO 96/22770. Appellants believe they are pioneers in this field, being the first to discover use of a compound which inhibits the production, transcription, translation or activity of the 14 kDa PLA₂ enzyme for the treatment of chronic diseases having an angiogenic component to them.

By claiming a method of treatment by administering a compound that inhibits the 14 kDa PLA₂ enzyme, Appellants submit that they are claiming no more than that to which they are entitled under the law.

Accordingly, Appellants respectfully submit that the rejections of Claims 1 to 4, 7 to 9, and 13 to 17 under 35 U.S.C. § 112, first paragraph are improper.

CONCLUSION

In view of the foregoing, it is respectfully submitted that the final rejection of Claims 1 to 4, 7 to 9 and 13 to 17 in this application is in error and should be reversed.

Respectfully submitted,

By:

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APPENDIX

CLAIMS ON APPEAL, U.S.S.N. 09/142,983

1. A method of treating a chronic disease in a mammal in need thereof, which disease is characterized by excessive, undesired or inappropriate angiogenesis, with an effective amount of a compound which inhibits the production, transcription, translation or activity of 14 kDa PLA₂ and wherein the compounds were invented after the priority date of March 26, 1996.

2. The method according to Claim 1 wherein the disease is diabetic retinopathy and other ocular neovascularizations.

3. The method according to Claim 1 wherein the disease is tumor growth and metastasis.

4. The method according to Claim 1 wherein the disease is atherosclerosis.

7. A method of treating a chronic disease of diabetic retinopathy or ocular neovascularization in a mammal in need thereof, which disease is characterized by excessive, undesired or inappropriate angiogenesis with an effective amount of a compound which inhibits the production, transcription, translation or activity of 14 kDa PLA₂ and wherein the compounds were invented after the priority date of March 26, 1996.

8. A method of treating a chronic disease of tumor growth and metastasis in a mammal in need thereof, which disease is characterized by excessive, undesired or inappropriate angiogenesis with an effective amount of a compound which inhibits the production, transcription, translation or activity of 14 kDa PLA₂ and wherein the compounds were invented after the priority date of March 26, 1996.

9. A method of treating a chronic disease of atherosclerosis in a mammal in need thereof, which disease is characterized by excessive, undesired or inappropriate angiogenesis with an effective amount of a compound which inhibits

which inhibits the production, transcription, translation or activity of 14 kDa PLA₂ and wherein the compounds were invented after the priority date of March 26, 1996.

13. A method of treating a chronic disease in a mammal in need thereof, which disease is characterized by excessive, undesired or inappropriate angiogenesis, with an effective amount of a compound which inhibits the production, transcription, translation or activity of 14 kDa PLA₂ other than those compounds disclosed before March 26, 1996.

14. A method of treating a chronic disease in a mammal in need thereof, which disease is characterized by excessive, undesired or inappropriate angiogenesis, with an effective amount of a compound which inhibits the production, transcription, translation or activity of 14 kDa PLA₂ and wherein the compound was used before or invented after the priority date of March 26, 1996.

15. A method of treating a chronic disease of diabetic retinopathy or ocular neovascularization in a mammal in need thereof, which disease is characterized by excessive, undesired or inappropriate angiogenesis with an effective amount of a compound which inhibits the production, transcription, translation or activity of 14 kDa PLA₂ and wherein the compound was used before or invented after the priority date of March 26, 1996.

16. A method of treating a chronic disease of tumor growth and metastasis in a mammal in need thereof, which disease is characterized by excessive, undesired or inappropriate angiogenesis with an effective amount of a compound which inhibits the production, transcription, translation or activity of 14 kDa PLA₂ and wherein the compound was used before or invented after the priority date of March 26, 1996.

17. A method of treating a chronic disease of atherosclerosis in a mammal in need thereof, which disease is characterized by excessive, undesired or inappropriate angiogenesis with an effective amount of a compound which inhibits which inhibits the production, transcription, translation or activity of 14 kDa PLA₂ and wherein the compound was used before or invented after the priority date of March 26, 1996.